

**REMARKS**

**Rejection of Claims Under 35 U.S.C. 102**

Claims 1-4 and 31 stand rejected under 35 U.S.C. 102 for allegedly being anticipated by U.S. Patent No. 6,406,498 to Tormala (the '498 patent). Applicants traverse this rejection. Claim 1 recites a multifunctional synthetic bioabsorbable device comprising solid particles of a pharmacological agent. The Examiner states that according to U.S. Patent No. 6,579,533, bioactive glass is anti-bacterial and thus the bioactive glass is considered a pharmaceutical agent. Bioactive glasses belong to a group of bioceramics that are used as biomaterials (See Exhibit A). Although some bioactive glasses have anti-bacterial properties, they are not considered "pharmacological agents" as that term is understood by one in the art. "Pharmacological" is an adjective derived from the word "pharmacology," which according to the New Oxford Dictionary of English (Clarendon Press, Oxford 1998) is "the branch of medicine concerned with the uses, effects and modes of action of drugs." (See Exhibit B). Bioactive glasses are biomaterials not drugs. As such, a bioactive glass is not a "pharmacological agent" as recited in claim 1. Accordingly, Applicants submit that claim 1 (and all claims that depend therefrom) are not anticipated by the '498 patent and Applicants request withdrawal of this rejection.

**Rejection of Claims Under 35 U.S.C. 103**

Claims 1-26 and 31 stand rejected as being allegedly rendered obvious by EP 1157708 to Fischer ("Fischer") in view of the '498 patent. Fischer states that antimicrobial agents should not undergo chemical degradation or modification, or loss of anti-microbial properties under processing conditions. (*See e.g.* page 3, lines 22-24). However, there is no teaching or suggestion that the a pharmacological agent should retain its solid particulate form in the melt-processing of the matrix as recited in claim 1. Therefore, it would not be obvious to produce a multi-functional bioabsorbable device which comprises a pharmaceutical agent and cavities around the solid particles of the pharmaceutical agent dispersed in a synthetic bioabsorbable oriented polymer matrix as recited by claim 1. Accordingly, Applicants submit that claim 1 (and all claims that depend therefrom) are not rendered obvious by the combination of the '498 patent and Fischer and Applicants request withdrawal of this rejection.

**Conclusion**

It is respectfully submitted that the present application is now in condition for allowance, which action is respectfully requested. The Examiner is invited to contact Applicants' representative to discuss any issue that would expedite allowance of the subject application.

Any fees for extension(s) of time or additional fees that are required in connection with the filing of this response are hereby petitioned under 37 C.F.R. § 1.136(a), and the Commissioner is authorized to charge any such required fees or to credit any overpayment to Kenyon & Kenyon LLP Deposit Account No. 11-0600.

Respectfully submitted,

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## Bioceramics

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Ceramics used for the repair and reconstruction of diseased or damaged parts of the musculo-skeletal system, termed bioceramics, may be bioinert (e.g., alumina and zirconia), resorbable (e.g., tricalcium phosphate), bioactive (e.g., hydroxyapatite, bioactive glasses, and glass-ceramics), or porous for tissue ingrowth (e.g., hydroxyapatite-coated metals). Applications include replacements for hips, knees, teeth, tendons, and ligaments and repair for periodontal disease, maxillofacial reconstruction, augmentation and stabilization of the jaw bone, spinal fusion, and bone repair after tumor surgery. Pyrolytic carbon coatings are thromboresistant and are used for prosthetic heart valves. The mechanisms of tissue bonding to bioactive ceramics have resulted in the molecular design of bioceramics for interfacial bonding with hard and soft tissue. Bioactive composites are being developed with high toughness and elastic modulus that match with bone. Therapeutic treatment of cancer has been achieved by localized delivery of radioactive isotopes via glass beads. Clinical success of bioceramics has led to a remarkable advance in the quality of life for millions of people.

### 1. Introduction

MANY millennia ago, the discovery that fire would irreversibly transform clay into ceramic pottery led to an agrarian society and an enormous improvement in the quality and length of life. Another revolution has occurred in the use of ceramics during the past four decades to improve the quality of life. This revolution is the innovative use of specially designed ceramics for the repair, reconstruction, and replacement of diseased or damaged parts of the body. Ceramics used for this purpose are termed "bioceramics." Bioceramics can be polycrystalline (alumina or hydroxyapatite), bioactive glass, bioactive

glass-ceramic (A/W), or bioactive composite (polyethylene-hydroxyapatite).

Many specialty ceramics and glasses have been developed during this century for use in the health care industry, e.g., eyeglasses, diagnostic instruments, chemical ware, thermometers, tissue culture flasks, fiber optics for endoscopy, and carriers for enzymes and antibodies.<sup>1</sup> Ceramics also are used widely in dentistry as restorative materials, gold porcelain crowns, glass-filled ionomer cements, dentures, etc. The materials used in these applications are called dental ceramics.<sup>2</sup>

This review is devoted to the use of bioceramics as implants to repair parts of the body, usually the hard tissues of the musculo-skeletal system, such as bones, joints, or teeth, although use of carbon coatings for replacement of heart valves also is included. Many ceramic compositions have been tested for use in the body;<sup>1,3</sup> however, few have achieved human clinical application. Clinical success requires the simultaneous achievement of a stable interface with connective tissue and a match of the mechanical behavior of the implant with the tissue to be replaced. Only the few bioceramics that meet these severe requirements for clinical success are emphasized in this review. Historical developments of bioceramics have been presented by Hulbert *et al.*<sup>3</sup>

#### (1) Need for Bioceramics

Bioceramics are needed to alleviate pain and restore function to diseased or damaged parts of the body. A major contributor to the need for "spare parts" for the body is the progressive deterioration of tissue with age. Bone is especially vulnerable to fracture in older people because of a loss of bone density and strength with age.<sup>4</sup> Figure 1 summarizes the effect of time on bone strength and density from the age of 30 years onward. The effect is especially severe in women because of hormonal changes associated with menopause. Bone density decreases because bone-growing cells (osteoblasts) become progressively less productive in making new bone and repairing microfractures. The lower density greatly deteriorates the strength of the porous bone, called trabecular or cancellous bone (Fig. 2), in the ends of long bones and in vertebrae. An unfortunate consequence is that many old people fracture their hips or have collapsed vertebrae and spinal problems.

The great challenge facing the use of ceramics in the body is to replace old, deteriorating bone with a material that can func-

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centennialfeature

The Pharisees are mentioned only by Josephus and in the New Testament. Unlike the Sadducees, who tried to apply Mosaic law strictly, the Pharisees showed some freedom of interpretation. Although in the Gospels they are represented as the chief opponents of Christ, they seem to have been less hostile than the Sadducees to the nascent Church, with which they shared belief in the Resurrection.

**DERIVATIVES** *Pharisaic* /fari'senk/ adjective, *Pharisaical* adjective, *Phariseism* /fari'seiz(ə)m/ noun.

**ORIGIN** Old English *fariseus*, via ecclesiastical Latin from Greek *Pharisaios*, from Aramaic *parisaya* 'separated ones' (related to Hebrew *parits* 'separated').

**pharmaceutical** /fɑ:mə'sju:t(ə)kəl/ adjective of or relating to medicinal drugs, or their preparation, use, or sale.

**noun** (usu. *pharmaceuticals*) a compound manufactured for use as a medicinal drug.

**pharmaceuticals** shares in companies manufacturing medicinal drugs.

**DERIVATIVES** *pharmaceutically* adverb, *pharmaceutics* plural noun.

**ORIGIN** mid 17th cent.: via late Latin from Greek *pharmakutikos* (from *pharmakutēs* 'druggist', from *pharmakon* 'drug') + *-al*.

**pharmacist** *noun* a person who is professionally qualified to prepare and dispense medicinal drugs.

**pharmaco-** /fɑ:mə'kəʊ/ combining form relating to drugs: *pharmacogenetics*.

**ORIGIN** from Greek *pharmakon* 'drug, medicine'.

**pharmacodynamics** *plural noun* (treated as sing.) the branch of pharmacology concerned with the effects of drugs and the mechanism of their action.

**DERIVATIVES** *pharmacodynamic* adjective.

**pharmacogenetics** *plural noun* (treated as sing.) the branch of pharmacology concerned with the effect of genetic factors on reactions to drugs.

**pharmacognosy** /fɑ:mə'kɒgnəsi/ *noun* (mass noun) the branch of knowledge concerned with medicinal drugs obtained from plants or other natural sources.

**DERIVATIVES** *pharmacognosist* noun.

**ORIGIN** mid 19th cent.: from *PHARMACO-* 'of drugs' + *gnosis* 'knowledge'.

**pharmacokinetics** *plural noun* (treated as sing.) the branch of pharmacology concerned with the movement of drugs within the body.

**DERIVATIVES** *pharmacokinetic* adjective.

**pharmacology** *noun* (mass noun) the branch of medicine concerned with the uses, effects, and modes of action of drugs.

**DERIVATIVES** *pharmacologic* adjective, *pharmacological* adjective, *pharmacologically* adverb, *pharmacologist* noun.

**ORIGIN** early 18th cent.: from modern Latin *pharmacologia*, from Greek *pharmakon* 'drug'.

**pharmacopoeia** /fɑ:mə'kɒpi:ə/ (US also *pharmacopeia*) *noun* a book, especially an official publication, containing a list of medicinal drugs with their effects and directions for their use.

**a** stock of medicinal drugs.

**ORIGIN** early 17th cent.: modern Latin, from Greek *pharmakopoiia* 'art of preparing drugs', based on *pharmakon* 'drug' + *-poios* 'making'.

**pharmacotherapy** *noun* (mass noun) medical treatment by means of drugs.

**pharmacy** *noun* (pl. *-ies*) a shop or hospital dispensary where medicinal drugs are provided or sold.

**a** (mass noun) the science or practice of the preparation and dispensing of medicinal drugs.

**ORIGIN** late Middle English (denoting the administration of drugs): from Old French *farmacie*, via medieval Latin from Greek *pharmakēia* 'practice of the druggist', based on *pharmakon* 'drug'.

**Pharos** /fə'roʊs/ a lighthouse, often considered one of the Seven Wonders of the World, erected by Ptolemy II (308–246 BC) in c.280 BC on the island of Pharos, off the coast of Alexandria.

**a** (as noun *a pharos*) a lighthouse or a beacon to guide sailors.

**pharyngeal** /fə'riŋ(dʒ)jəl, /fə'riŋ'dʒi:əl/ adjective of or relating to the pharynx.

**a** Phonetics (of a speech sound) produced by articulating the root of the tongue with the pharynx, a feature of certain consonants in Arabic, for example.

**noun** Phonetics a pharyngeal consonant.

**ORIGIN** early 19th cent.: from modern Latin

*pharyngeus* (from Greek *pharynx*, *pharyng-* 'throat') + *-al*.

**pharyngealizes** /fə'riŋ(dʒ)əlaɪz/ (also *-leez*) *verb* (with obj.) Phonetics articulate (a speech sound) with constriction of the pharynx.

**DERIVATIVES** *pharyngealization* noun.

**pharyngitis** /fə'riŋ'ɡɪtɪs/ *noun* (mass noun) Medicine inflammation of the pharynx, causing a sore throat.

**pharyngo-** /fə'riŋɡəʊ/ combining form of or relating to the pharynx: *pharyngotomy*.

**ORIGIN** from modern Latin *pharynx*, *pharyng-*.

**pharyngotomy** /fə'riŋ'ɡɒtəmi/ *noun* (pl. *-ies*) a surgical incision into the pharynx.

**pharynx** /fə'riŋks/ *noun* (pl. *pharynges* /fə'riŋ(dʒ)ɪz/) Anatomy & Zoology the membrane-lined cavity behind the nose and mouth, connecting them to the oesophagus.

**a** Zoology the part of the alimentary canal immediately behind the mouth in invertebrates.

**ORIGIN** late 17th cent.: modern Latin, from Greek *pharynx*, *pharyng-*.

**phascogale** /fə'skɒɡəli/ *noun* a small arboreal flesh- and nectar-eating Australian marsupial with a pointed snout, large eyes and ears, and a bushy tail.

**a** Genus *Phascogale*, family Dasyuridae: two species.

**ORIGIN** modern Latin, from Greek *phaskolos* 'purse' + *gale* 'weasel'.

**phase** /feɪz/ *noun* 1 a distinct period or stage in a process of change or forming part of something's development: the final phases of the war | [as modifier] phase two of the development is in progress.

**a** a stage in a person's psychological development, especially a period of temporary unhappiness or difficulty during adolescence or a particular stage during childhood: most of your fans are going through a phase. **a** each of the aspects of the moon or a planet, according to the amount of its illumination, especially the new moon, the first quarter, the full moon, and the last quarter. **a** each of the separate events in an evening competition.

**2** Zoology a genetic or seasonal variety of an animal's coloration.

**a** a stage in the life cycle or annual cycle of an animal.

**3** Chemistry a distinct and homogeneous form of matter (i.e. a particular solid, liquid, or gas) separated by its surface from other forms.

**4** Physics the relationship in time between the successive states or cycles of an oscillating or repeating system (such as an alternating electric current or a light or sound wave) and either a fixed reference point or the states or cycles of another system with which it may or may not be in synchrony.

**a** each of the electrical windings or connections of a polyphase machine or circuit.

**5** Linguistics (in systemic grammar) the relationship between a catenative verb and the verb that follows it, as in *she hoped to succeed and I like swimming*.

**a** a structure containing two verbs in such a relationship.

**verb** (with obj.) (usu. *be phased*) 1 carry out (something) in gradual stages: the work is being phased over a number of years | [as adj. *phased*] a phased withdrawal of troops.

**a** (phase something in/out) introduce into (or withdraw from) use in gradual stages: our armed forces policy was to be phased in over 10 years.

**2** Physics adjust the phase of (something), especially so as to synchronize it with something else.

**PHRASES** in (or out of) phase being or happening in (or out of) synchrony or harmony: the cabling work should be carried out in phase with the building work.

**ORIGIN** early 19th cent. (denoting each aspect of the moon): from French *phase*, based on Greek *phasis* 'appearance', from the base of *phainō* 'to show'.

**phase angle** *noun* Physics an angle representing a difference in phase, 360 degrees (2π radians) corresponding to one complete cycle.

**a** Astronomy the angle between the lines joining a given planet to the sun and to the earth.

**phase contrast** *noun* (mass noun) the technique in microscopy of introducing a phase difference between parts of the light supplied by the condenser so as to enhance the outlines of the sample, or the boundaries between parts differing in optical density.

**phase diagram** *noun* Chemistry a diagram representing the limits of stability of the phases in a chemical system at equilibrium with respect to variables such as composition and temperature.

**phase-locked** *verb* (with obj.) Electronics the frequency of (an oscillator or a laser) relative to a stable oscillator of lower frequency by a signal that utilizes a correction signal derived from phase difference generated by any shift in frequency.

**phase modulation** *noun* (mass noun) the variation of the phase of a radio or other wave means of carrying information such as an audio signal.

**phaser** *noun* 1 an instrument that alters a signal by phasing it.

**2** (in science fiction) a weapon that delivers a signal that can stun or annihilate.

**phase rule** *noun* Chemistry a rule relating possible numbers of phases, constituents, and degrees of freedom in a chemical system.

**phase shift** *noun* Physics a change in the phase of a waveform.

**phase space** *noun* Physics a multidimensional space in which each axis corresponds to one of a set of coordinates required to specify the state of a physical system, all the coordinates being represented so that a point in the space corresponds to a state of the system.

**phase velocity** *noun* Physics the speed of propagation of a sine wave or a sinusoidal component of a complex wave, equal to the product of its wavelength and frequency.

**phasic** /feɪzɪk/ adjective of or relating to a phase or phases.

**a** Physiology characterized by occurrence in a reflex rather than continuously: phasic and tonic reflexes.

**phasing** *noun* (mass noun) the relationship between the timing of two or more events, or the adjustment of this relationship: graphical tests were used to investigate the phasing of traffic lights.

**a** the modification of the sound signal from an acoustic guitar or other electronic instrument by introducing a phase shift into either of two copies of it and recombining them. **a** the action of dividing a task or process into several stages: the phasing of an overall project.

**Phasmoda** /fə'zɒdə/ 1 Entomology an order of insects that comprises the stick insects and leaf beetles. They have very long bodies that resemble twigs or leaves.

**2** Zoology a class of nematodes that includes parasitic hookworms and roundworms. Also *SECERNENTEA*.

**DERIVATIVES** *phasmodic* noun & adjective.

**ORIGIN** modern Latin (plural), from Latin *phasmoda* 'apparition', from Greek.

**phasor** /feɪzə/ *noun* Physics a line used to represent a complex electrical quantity as a vector.

**ORIGIN** 1940s: from *PHASE*, on the pattern of a *phant* /fæŋ/ adjective black slang excellent: a London with a really phat funk sound.

**ORIGIN** 1970s (originally used to describe a man in the sense 'sexy, attractive'): of uncertain origin.

**phatic** /fə'tɪk/ adjective denoting or relating to language used for general purposes of interaction, rather than to convey information or ask questions. Utterances such as *hello, how are you, and nice morning, isn't it?* are phatic.

**ORIGIN** 1920s: from Greek *phatos* 'spoken', *phatikos* 'affirming'.

**PhD** *abbreviation* for Doctor of Philosophy.

**ORIGIN** from Latin *philosophiae doctor*.

**pheasant** *noun* a large long-tailed game bird native to Asia, the male of which typically has showy plumage.

**a** Family Phasianidae: several genera and many species, including the common pheasant (*Phasianus colchicus*) which has been widely introduced for shooting.

**ORIGIN** Middle English: from Old French *phasian*, Latin from Greek *phasianos* 'bird of Phasis', the name of a river in the Caucasus, from which bird is said to have spread westwards.

**pheasantry** *noun* (pl. *-ies*) a place where pheasants are reared or kept.

**pheasant's eye** *noun* a plant of the buttercup